THE AMERICAN JOURNAL
OF
# OPHTHALMOLOGY.

VOL. XXV. MARCH, 1908. No. 3.

## ORIGINAL ARTICLES.

### THE PATHOLOGY OF THE RETINA IN BRIGHT'S DISEASE.

By N. M. Semple, M.D.,
ST. LOUIS.

Through the kindness of Professor Voelkers, and of Professor Heller, of the University of Kiel, I had the good fortune to be able to study both before and after death the eyes of three cases showing the typical retinitis of Bright's disease in its different stages of development. All three cases had been under observation for varying lengths of time in the ophthalmic clinic. Later, they were admitted to the general medical hospital, where death occurred as a direct result of uræmia. The value of the ocular material was also increased on account of the accurate general post-mortem findings, and also through the fact that the eyes were placed in the fixing solutions almost immediately after death, thereby insuring excellent and accurate reaction to the various stains.

The aim of the present article is to give the results of the microscopical study of the retinæ of the three cases which have led me to conclusions corresponding in many respects to those found in the literature on the subject and now generally accepted, yet also to other conclusions which differ from any that I have been able to find. Hence I have considered it worth while to make the following report. As the pathological changes

of the retina found in the three cases differ only in so far as they show different stages of progress of the disease, I shall describe them jointly.

The clinical and post-mortem findings are first briefly given:

CASE I.—R. Johann, age 30 years, factory laborer, on March 25, 1900, received in the medical clinic, giving history of swelling of both legs beginning on the 14th of the same month. During the last few days before admittance to the clinic, patient suffered with severe headaches and frequent vomiting. Had also complained of inability to read the newspaper. Physical examination gave the following: marked sallowness of skin (blood showing 60% of hæmoglobin), marked œdema of legs, hypertrophy of left ventricle with pounding heart-tones, increased blood-pressure (258 Riva-Rocci), urine abundant, circa 2000 cc. per diem with three to four tenths per cent albumin, and numerous casts of all kinds. Examination of fundi showed on both sides hyperæmia and swelling of discs, which were with difficulty distinguished from surrounding retinæ. Veins tortuous and distended, arteries practically normal. Especially about the discs, but also in the neighborhood of the maculæ, the retina was studded with the characteristic white plaques, but with no decided star-arrangement around the fovea. On April 10th, there appeared on the temporal side of the right disc numerous small punctate hæmorrhages—also beneath the disc of the left eye. On the eighth of May the patient died from uræmia. The post-mortem examination gave the following: parenchymatous nephritis of the left, parenchymatous and interstitial nephritis of the right kidney. Decided hypertrophy of the heart. Marked œdema and brown discoloration of the lungs. Some induration of the liver and spleen. Numerous ecchymoses in the walls of the stomach. Hyperæmia of the small and large intestines. Chronic meningitis.

CASE II.—S. Karl, age 19 years, house servant. On July 25th, 1900, received in medical clinic giving history of first swelling of both legs, followed by the symptoms of a slowly progressing uræmia. Examination showed marked swelling of both legs, skin wax-colored (40% hæmoglobin), decided hypertrophy of left ventricle, urine scanty (400-700cc. per diem), numerous hyaline and granular casts. The ophthalmoscope showed both discs indistinct in outline, veins tortuous, especially in the left disc. In both eyes were numerous yellowish-white plaques in macular region, typical star-formation around right macula. In

the left eye was found a large round glistening white exudate, directly in the macula, sharply differentiated from the surrounding yellowish-white plaques, and which later by the microscopical examination was found to be an exudate between retina and choroid, with a resultant circumscribed detachment of the retina. Death on August 10th, from uræmia. Post-mortem examination gave the following: very decided gray atrophy of the left kidney, less marked of the right. Chronic interstitial and parenchymatous nephritis of both kidneys. Decided œdema of the lungs and meninges. Indurated liver, spleen and pancreas. Hyperæmia and swelling of the walls of the stomach and intestines. Atrophy of both testicles. Slight chronic meningitis.

Case III.—Rosa K., 15 years old. On March 10th, 1901, received in medical clinic with the following incomplete history: Had had an attack of pleurisy in 1897, since which time had always suffered from "kidney trouble". Vision began to fail about the beginning of March. Later frequent bleeding from the nose. Patient suffered from decided shortness of breath. Examination discovered a slight enlargement of the heart to the left. Very hard pulse. Urine showed seven-tenths per cent albumin with hyaline casts. The ophthalmoscopic findings were somewhat more complete; extending from the disc to the macula was a ring of irregular white plaques which surrounded both the disc and macula. In the area of this ring of white exudate, the blood-vessels were often well defined, sometimes indistinct in outline, sometimes completely covered. Numerous hæmorrhages along the course of the vessels. Complete central scotomata. Death of patient on March 29. Post-mortem examination showed high grade anæmia, decided atrophy of both kidneys, deep scar diagonally through the right kidney, hypertrophy of the heart, especially of the right ventricle, small endarteriitis plaques in arcus and aorta, thickening of lungs, very hard liver, light follicular swelling of the spleen, hard suprarenal bodies, hard pancreas, decided hyperæmia, and in parts, slate-like discoloration of small intestines, with follicular swelling increasing downwards. Very decided œdema of colon.

Both globes from Case I. were enucleated immediately after death, the sclera carefully dissected from the posterior half, after which they were hardened in Flemming's solution. After a rapid subsequent hardening in alcohol of increasing strength, they were divided equatorially and the posterior halves free of sclera, carefully imbedded in paraffin through chloroform, and

cut in serial sections. The globes from Cases II. and III. were handled somewhat differently. Immediately after death a warm 20% formalin solution was injected by means of a small Pravatz syringe directly into the vitreous as near the disc as possible from the nasal side. At the post-mortem made a few hours later, the globes were enucleated, the sclera removed from the posterior half and further handled in formalin. After the usual subsequent hardening in alcohol, the eyes were divided equatorially, the posterior halves imbedded in paraffin from which serial sections were made.

It might be here remarked that the post-mortem findings show in Case I. a neuro-retinitis associated with changes in the kidney more of an acute parenchymatous type, while in the other two cases the renal condition is a chronic interstitial nephritis with a small atrophied kidney.

The pathology of the retina as shown by the sections of all three cases presents a uniform, definite picture. The changes are to be found chiefly in the outer recticular layer, but also, in a lesser degree, in the inner nuclear layer, in the ganglion cell and nerve fibre layers, and corresponding to the ophthalmoscopic picture, are confined almost entirely to the region of the macula and the disc. The changes that are especially marked in the outer reticular layer may be considered under two heads: 1. The peculiar formation of cyst-like spaces, so often described, which show as a rule no visible contents except an occasional degenerated cell lying free in the center, while in other places the spaces are seen to be filled with an almost transparent finely fibrinous fluid. These spaces are also found throughout the entire thickness of the swollen retina, and may be considered the first stage of the pathologic process. Their relation to the other more characteristic changes will be considered more in detail later. Under the second head may be described those changes which are seen as more or less extensive deposits arranged in irregular masses which are found largely, almost exclusively, in the outer recticular layer, often involving the entire thickness of this layer, and in certain places extending through the outer nuclear layers, as far as the external limiting membrane. Concerning the nature and origin of these masses, there exists in the literature a decided difference of opinion, at least an uncertainty of expression in regard to them. By Leber they are described as large very irregular plaques or masses of colloidal appearance which contain degenerated nuclei or cells or retinal neuroglia fibres, partly derived from the coagulation of albuminous

fluid, the result of the reaction of the fixing reagents. Leber also described an extensive deposit of fat-cells with a fatty infiltration of the supporting fibres of the retina. Karl Theodore described the process as a coagulation necrosis, caused chiefly by the local anæmia, without going into further details as to the exact nature of the masses. They are considered by Haab as lumps of fat-cells, also as irregular aggregations of a material resembling colloid, in all probability the product of extravasations of blood. v. Michel suggests that, in certain cases, the exudate is a fibrin-coagulum. But he says that the ophthalmo-

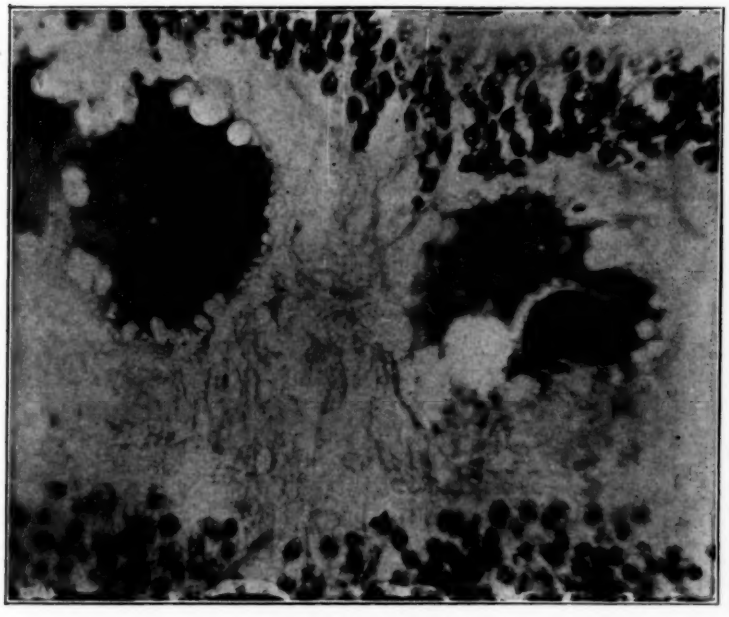

ILLUSTRATION I.
**Hyaline masses in external reticular layer. Benda's iron-hæmotoxylin stain, showing the different stages of metamorphosis.**

scopic appearance of the retina is entirely due to nutritional disturbances, resulting from the hyaline degeneration of the walls of the smallest arteries, which disturbances show themselves as an extensive fatty degeneration, and deposits of fat cells in large masses,—also a fatty infiltration of the supporting fibres of Mueller. In addition to the fat he also finds hyaline degeneration of the supporting fibres and colloid-like masses in the intervening spaces. But the pathology of the retina is considered by him to be due entirely to the extensive changes in the walls of the retinal and choroidal capillaries, whereby the nutrition of those layers of the retina dependent on these capillaries is so dis-

turbed, that a fatty degeneration, with deposits of large masses of fat cells, takes place.

A study of my specimens leads me to a different conclusion: the white plaques as seen by the ophthalmoscope in the papillo-macular area are shown to be masses of exudate confined largely to the outer reticular layer, which may be divided into three definite stages: first, exudates which show a glistening homogeneous strongly refractive appearance, often surrounded by masses of blood-corpuscles; second, similar exudates, which are not entirely homogeneous, but in which are found numerous minute often sharply differentiated small round bodied which resemble fat-cells in appearance, but which, as is shown by farther examination, do not contain the slightest indication of fat. After exposure to the action of the strongest mineral acids (concentrated hydrochloric acid for forty-eight hours) the masses remain unchanged. The strongest alkalies (potassium hydrate) have no effect on them. They dissolve neither in chloroform nor ether. They also possess a strong reaction to stains, especially for certain aniline stains. By eosin and acid fuchsin, the homogeneous substance stains bright red, while the small round bodies contained in the masses take on a deep red tone. According to the iron-hæmatoxylin method of Benda the small bodies stain an intense black, while the surrounding substance takes up the stain to a less degree. By eosin-hæmatoxylin, the masses are stained bright red, while the nuclei of the surrounding normal tissue show the usual blue reaction. The small bodies contained in the masses are stained a deeper red. The Weigert's gentian-violet method gives to the amorphous masses a dark blue tone. With potassium iodide, they are stained yellow like the surrounding tissue, nor does methyl-violet give the characteristic reaction for amyloid. To the von Gieson stain (a double stain with hæmatoxylin and picric-acid-fuchsin) the masses react in the following very characteristic way: the small bodies contained in the exudate take on a dark brown tone while the surrounding substance is stained a bright glistening red. Occasionally the amorphous masses are tinged slightly yellow by the picric acid. I have gone into such detail as to the reactions of these masses of exudate to the different reagents and stains, in order to show that they correspond in almost every particular to the substance first thoroughly described by v. Recklinghausen and designated by him as "Hyaline". The properties both chemical, and as regards the reaction to the aniline stains, which v. Recklinghausen demands for hyaline, are

shown to a very large degree by the above described substance. That it does not correspond in every particular need not be considered strange. As v. Recklinghausen himself admitted, the reaction of hyaline is, to a certain degree, variable. The yellow tone after exposure to picric acid solution, Fuchs observed in the pinguecula, also that under certain conditions hyaline is stained intensely by hæmatoxylin, as I found to be especially the case after Benda's method. That hyaline is often formed in irregular masses, in which are contained numerous small bodies which react more intensely to certain stains, has been observed by Fuchs in the pinguecula, later by A. Birch-Hirschfeld in corneal scars, indicating different stages of metamorphosis. The latter lays especial stress on the reaction of hyaline to the von Gieson stain. Ernst even goes so far as to claim that the origin of hyaline can be determined by the intensity of its reaction to this stain. Even if this is not the case, the picture obtained after staining with von Gieson's method is very characteristic. In regard to the way in which the hyaline is formed in extravasations, von Recklinghausen says that it is derived from the colorless elements of the blood and certain cells (e. g. Wanderzellen). That we have here in the retina a similar process is very easy to believe. This is all the more probable, as, without exception, there are found around the amorphous masses, cells of epitheloid appearance (probably migrating cells from the capillaries), and leucocytes in various stages of degeneration. The opinion that a degeneration of the fixed tissue cells is necessary for the formation of hyaline, is not considered well-grounded by Fuchs. For instance, he claims that neither the amorphous masses in the conjunctiva (pinguecula), nor the concrements found in the arcus senilis are derived from the degenerated tissue-cells, that, on the contrary, they lie between the normal fibres of the conjuctiva and cornea. As regards the outer reticular layer of the retina it is impossible that the degeneration of the fixed tissue-elements play a part in the formation of the hyaline, as here the amorphous masses lie between the thickened supporting fibres of the retina (which are thereby shoved apart) and the cells in the two adjacent granular layers show no pathological changes.

The third form in which the exudate is found, and which in the specimen is not so often seen as the above, presents a charartistic fibrillar net-like appearance. By means of Weigert's specific aniline-gentian violet stain one obtains such a characteristic picture of fibrin that there remains no doubt of the fibrinous nature of the exudate. In other places, on the contrary, the pic-

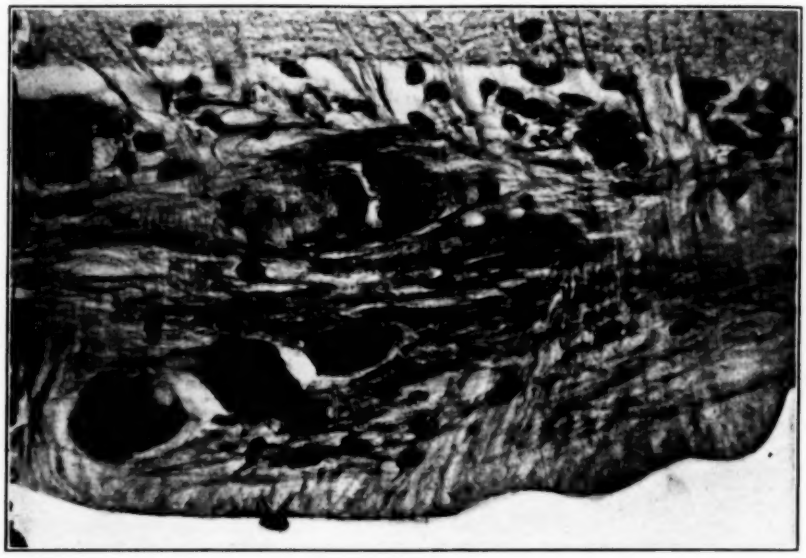

ILLUSTRATION II.

**Ganglion-cells in various stages of swelling and degeneration, displaced into nerve fibre layer, reaching internal limiting membrane. Benda's iron-hæmotoxylin stain.**

ILLUSTRATION III.

**Same as Illustration II. v. Gieson stain.**

ture is much less characteristic. The network loses its fine fibrillar apearance, the lines becoming heavier, and often much thicker, the meshes being filled with a transparent fluid. The gentian-violet stain no longer gives the characteristic reaction for fibrin, while the response to the other stains is much more pronounced. Eosin and fuchsic acid give a light stain to this form of the exudate, which also shows a strong resistance to the action of acids and alkalies. In order to explain this, one must agree with the opinion of Weigert, that fibrin changes into hyaline. The substance just described can be considered as the first transitional stage. It is generally admitted that hyaline is to be found in various forms. v. Recklinghausen indeed says that it is indeed very uncertain that we have not to do with a conglomeration or mixture of various bodies. That fibrin, by a process of gradual metamorphosis, changes into hyaline offers the most probable explanation of the changes in the retinal exudation, the last form described being the first step in the process of this metamorphosis, which eventually results in the formation of the homogeneous hyaline masses.

In addition to the above pathologic changes which I have described in such detail, the sections of the retinæ of all three cases show certain very interesting conditions, which seem to be very characteristic of this peculiar form of retinitis, and which have been considered and described as varicosities of the axis-cylinder processes in the nerve-fibre layer, since the original work on the subject by Heinrich Mueller. The first account of these changes was attempted by Heymann and Zenker in 1855, who described masses which they thought lay in the ganglion cell layer, which were made up of ganglion cells in various stages of fatty degeneration, and also numerous cells with one process only, which contained small fat-cells, and in addition a very pale granular substance with glistening sharply contoured nuclei without nucleoli. Virchow also described similar glistening bodies which he considered sclerosis of the ganglion cells (Sclerose der Ganglionzellen). In a later article Wagner agreed with Virchow. In 1855 Heinrich Mueller published a more detailed and exact description of these changes which he claimed were confined entirely to the nerve-fibre layer and therefore could not be ganglion-cells. He described nests of darkly contoured bodies closely resembling ganglion-cells and which he considered as the same bodies described by Zenker and Virchow, but which were never to be found in the ganglion-cell layer, on the con-

trary in the nerve-fibre layer, and which he therefore considered, on account of their position, shape, etc., as hypertrophies or varicosities of the nerve-fibres themselves and not in any way ganglion-cells. Since this publication of Mueller these changes have been generally accepted as described by him. Haab in his atlas shows illustrations of enormously swollen axis-cylinders. In all of the modern text-books, this view has been accepted by the writers. Karl Theodore casually suggests the possibility of a regressive metamorphosis of the leucocytes and of the red-blood-corpuscles playing a part in the formation of these masses. The study of these changes as shown by my specimens leads to conclusions, both as to their origin and nature, which differ from those just described. There is no doubt that they are the same as those given in detail by Mueller, the position and general appearance coinciding exactly with his description, and since his time, with the illustrations found in the different works on the subject. That we have here to do with varicosities or thickenings of the nerve-fibres is on close study shown to be impossible. In following the serial sections, nowhere could it be found that the nerve-fibre extended in both directions from its so-called varicosity. In their reaction to the various aniline-stains, the masses, if we may term them such, show at first glance a remarkable resemblance to the exudate found in the outer reticular layer. The von Gieson stain gives the following picture: the resemblance in form to ganglion-cells is very striking (illustration 3). Sometimes in the center, sometimes more or less toward the periphery of what would represent the cell-body, is found, as a rule, one, occasionally two, small bodies, stained a dark red, which could well represent the nucleus of a degenerated cell. This central body is always sharply differentiated from the surrounding cell-substance, which latter stains a light yellowish-red and possesses an entirely hemogeneous appearance. By the combined eosin-hæmatoxylin stain, the central body takes on an intensely red color while the surrounding cell-substance is a light red. Towards other stains (carmine, fuchsin, etc.), the bodies react in a way similar to the reaction shown by the exudate found in the outer reticular layer. In other words, we have bodies possessing the characteristic form of ganglion-cells but which show not the slightest resemblance either to the cell-substance or to the nucleus of a ganglion cell in their reaction to the various stains. Yet the longer the preparations are studied the more is one convinced that one has

to do with masses of degenerated ganglion-cells which have been forced from their normal position in the ganglion layer into the nerve-fibre layer, often as far as the internal limiting membrane. There are many things shown by the specimens which prove this to be the correct view. The bodies, as was originally observed by Mueller, are found only in nests or masses, which are made up often of enormously swollen bodies sometimes showing a diameter, as observed by Mueller, of 0.015 mm. I have found them as large as 0.03 mm. in diameter. In Case I. where the sclera was removed from the posterior part of the globe and the hardening carried out in Fleming's solution and serial sections of 2½ to 5 microns made, it can be easily seen, that the nests are composed entirely of displaced ganglion-cells. In many places one sees where all of the cells of the ganglion-cell layer have been forced from their normal position into the nerve-fibre layer, shoved between the fibres often to the internal limiting membrane, leaving the ganglion-cell layer absolutely free of its normal supply of cellular elements. In the first stages of the process, the cells are to be found more or less in their normal position, they are somewhat swollen and have lost the characteristic appearance of a normal cell. The Nissl bodies are found near the cell-membrane, the cell-substance shows sometimes a fine fibrillar, sometimes a homogeneous appearance, resembling the changes described by Bach in the ganglion cells after artificial sublatio retinæ. As soon as the cells are forced between the axis-cylinders of the nerve-fibre layer, they become greatly swollen often with difficulty differentiated from the surrounding œdema, which œdema, as shown by farther investigation, is the actual cause of this swelling and displacement of the ganglion-cells. The thorough soaking of the cell by the exudate, and the pathologic changes of the cell-body incident thereto, offer the only explanation of the action of these bodies to the various stains. As described, they show practically the same reaction to the v. Gieson stain, to eosin-hematoxylin, carmine, etc., as does the exudate in the outer reticular layer. In other words, these changes are of the same nature as those found in other layers of the retina, the ganglion-cells becoming permeated and forced from their normal position by the œdema, eventually degenerating more or less completely into hyaline. The explanation of the fact, as shown by the preparations, that the ganglion-cells are always displaced inward into the nerve-fibre layer, is to be found in the anatomical arrangement of the smaller blood-vessels of

the retina. According to Greef, in the last edition of the Graefe-Saemisch Handbook, the larger vessels of the retina ordinarily lie equally enclosed on all sides by a rather thick bundle of nerve-fibres. The lateral branches take for the most part a perpendicular direction to the course of the nerve-fibres. It is then in the nerve fibre layer that the division into the larger branches takes place. Eventually from these are derived the retinal branches which are given off in a perpendicular direction to the inner surface of the retina and which form at various depths capillary plexuses. Of these one can differentiate two, the inner, larger meshed plexus lies in the inner reticular layer near the inner border of the inner nuclear layer. It is developed directly from the larger vessels. From this is developed a second outer plexus, which lies at the outer border of the inner nuclear layer and the inner border of the outer reticular layer. From this outer plexus are developed the veins. In the albuminuric retinitis, the œdematous exudate into the retina takes place from these two capillary plexuses, chiefly from the outer, where are to be found the smallest capillaries, in which the first effect of the disease is shown. As Bright's disease is generally considered to be primarily a pathologic condition of the blood, which has its first effect on the walls of the smallest blood vessels (of the brain, kidney, etc.) we may well so consider the process here in the retina. Directly in the outer terminal plexus of the retinal vessels is to be found the most favorable site for the pathologic process. As a result, we find the retinal disturbances most pronounced in that region which depends for its nourishment on the vessels of this outer plexus. The same condition prevails in the inner plexus, only in a less degree. The extravasation comes from this inner larger plexus, i. e., from the inner border of the inner reticular layer, forces itself through the ganglion-cell layer into the nerve fibre layer, and as a result, carries the ganglion cells out of their normal layer, shoving them between the axis-cylinder processes and at the same time thoroughly permeating the cell itself with the fluid of the exudate. Hence follows the enormous swelling of the cell body and the resultant displacement. Occasionally one can clearly follow through a series of sections the axis-cylinder processes in one direction only, e. g., toward the nerve-head. Here I should like to state, that it was not possible in a single instance to find a varicosity of a nerve fibre where one could follow the normal fibre in both directions from the swelling. In the ganglion cell layer it-

self, one finds the cells in the earliest stages of degeneration. They are often swollen to double their normal size, the cell substance loses its normal appearance, the Nissl bodies lie directly against the cell-membrane. Sometimes the nucleus is found near the periphery of the cell, often lying directly against the limiting membrane. Occasionally are found ganglion-cells in which the pathological changes are more advanced, showing the homogeneous or finely granular appearance, a change formerly described as hydropathic swelling. Here I should like to emphasize the fact that not in a single instance could fat be demonstrated in the ganglion-cells, not even in those that were carefully handled in osmic acid. Nor could there be found any fatty degeneration of the supporting fibres of Mueller. The supporting fibres are often thickened and elongated, the result of the inflammation and swelling of the retina.

As regards the other changes in the retina, the specimens offer little of interest. The rods and cones are as a rule well preserved, only in one place (Case II. O. S.) did I find extensive destruction caused by a large exudate between the rods and cones and the pigment layer of the retina, resulting in a detachment of the retina at this point. The exudate lay directly in the macula and corresponded exactly with the glistening white exudate as shown by the ophthalmoscope. The substance was fibrinous in character, showing in part, hyaline-metamorphosis. The outer nuclear layer shows as a rule very little change. Occasionally the exudate from the outer reticular layer extended through the nuclear layer to the external limiting membrane. Cystic spaces are present in small numbers. In the third case one finds in a few places hæmorrhages extending to the external limiting membrane. In the inner nuclear layer, the general appearance is one of an extensive œdema around the capillaries. The following picture is often seen: around the capillary is a zone entirely free from cells, giving the definite impression that an exudate had occurred from the capillary carrying with it the cells around the vessel, thereby allowing the supporting fibres to come into bold relief. The extensive changes in the walls of the blood-vessels as variously described in the literature especially by Karl Theodore and v. Michel, who considered the pathological condition as due to changes in the vessels entirely, which were found often entirely obliterated and changed into hyaline, were not to be found in my three cases. It is true that the walls of the capillary were often thickened, showing a homogeneous

appearance and a reaction to stains of a kind to indicate a hyaline degeneration. In only one place did I find a complete obliteration of the lumen of the vessel with a mass of tissue giving the hyaline reaction—a condition often found in the capillaries of the kidney.

The changes in the nerve head were of the kind indicating the general character of the pathological process, that is to say, a general œdema of the tissues of the nerve resulting often in free spaces, which in the hardened specimen show no visible fluid. The nerve fibres are so separated by this fluid that the spaces are frequently very marked. An infiltration of leucocytes is to be found especially in the neighborhood of the lamina cribrosa. The connective tissue is thickened, occasionally showing a marked reaction to the various stains. Neither a thrombosis of the central artery of the retina nor the numerous small thromboses of smaller vessels were to be found (as observed by Karl Theodore and von Michel).

The choroid shows the changes in the blood-vessels which were first described by Heinrich Mueller and later very thoroughly by Karl Theodore, but as regards these changes in the wall of the vessels, I was able to find neither those of the extensive type as described by the above-named investigator nor the marked changes described by v. Michel, especially of the veins which he designated as arteriitis or phlebitis proliferans, eventually obliterans. Especially is this the case in the retina where the apparent changes in the retinal vessels were slight as compared with the very marked and extensive changes in the retina itself. The study of the condition here rather leads to the conclusion that in Bright's disease we have to do with a disease chiefly and primarily of the blood itself which reacts on the walls of the smallest vessels, producing in various parts of the body eventually changes, whereby the albuminous constituents of the blood and often the cellular elements of the blood, are allowed to escape into the surrounding tissue, resulting, as in the case of the retina, in a violent inflammation with the pathologic changes described above. The retina, where the opportunity for such a process is especially favorable, is often the first seat of these changes. The fact that the masses of exudate are to be found chiefly in the outer reticular layer, and that this layer has its characteristic arrangement around the macula, the so-called Henle's layer, offers the most reasonable explanation of the frequent occurrence of the star figure around

the macula, which is considered so characteristic of the retinitis of Bright's disease.

Since writing the above manuscript, the publication of which had been delayed for several years, I find that F. Schieck, in a paper read before the Ophthalmological Society at Heidelberg, agrees with me that it is impossible to explain the pathology of the retina on the ground of a disturbance of nutrition resulting directly from changes in the walls of the blood-vessels—the view held by v. Michel Karl Theodor, Wehrli, Hofmann, Weeks, and others.

It is especially to be noticed that the three cases included in this report are all cases in which the longest duration of the retinitis, as obtained from the history, was not over four weeks. In this fact is to be found the probable explanation of the lack of any evidence of a deposit of fat or even of a beginning fatty degeneration, as well as of the existence of changes of any marked degree in the blood vessels. This would lead to the conclusion that both the extensive arterial changes and the deposit of fat so often found, are secondary changes, in no way especially typical of the retinitis of Bright's disease.

## LITERATURE.

1. Bach: Die Nervenzellenstructur der Netzhaut in Normalen und Pathologischen Zustænden. v. Graefe's Archiv. 41-iii s. 62.

2. Birch-Hirschfeld: Beitrag zur Kenntniss der Degenerativen Processe in Hornhautnarben. v. Graefe's Archiv. 48-ii s. 328.

3. Ewald: Ueber die Verænderungen Kleiner Gefæsse bei Morbus Brightii, etc. Virchow's Archiv. lxxi. 1877.

4. Fuchs: Zur Anatomie der Pinguecula. v. Graefe's Arch. 37 s. 143. Lehrbuch der Augenheilkunde.

5. Gurwitsch: Ueber Hyaline Bildungen im Sehnervenkopfe, und in der Netzhaut bei Morbus Brightii. Centralblatt fuer prakt. Augen. 1891 s. 225.

6. Haab: Atlas der Ophthalmoscopie.

7. Heymann: Ueber Amaurose bei Morbus Brightii und Fettdegeneration der Retina. v. Graefe's Archiv. 2-ii s. 142.

8. Hoffmann: Ein Beitrag zur Kentniss der Gefæssverænderungen im Auge bei Chronischer Nephritis, etc. Inaug. diss. Marburg und Archiv. fuer Augenheil. xliv s. 339.

9. Karl Theodor: Ein Beitrag zur Patholog. Anatomie des Auges bei Nierenleiden. 1887.

10. Koppen: Ein Beitrag zur Kentniss der Patholog. Anatomie bei Chronischer Nephritis. Inaug. Diss. Marburg.

11. Leber: Die Retinitis bei Nierenleiden. Graefe-Saemisch Handbuch der Augenheilkunde.

12. Litten: Ueber Verænderungen der Ret. bei Neph. Muench. Med. Wochenschrift.

13. v. Michel: Ueber Erkrankung der Gefæss-Systems der Arteria und Vena Centralis Retinæ, etc. Zeitschrift fuer Augenheilkunde. Bd. ii s.t. 1898.

Douzieme Congres International des Sciences Medicales. Annales d'Oculistique. T. cxviii. p. 288, in Lehrbuch der Augenheilkunde.

14. Mueller, H.: Anatomische Beitræge zur Ophthalmologie. v. Graefe's Archiv. 4-ii s. 41.

15. Opin et Rochon Duvigneaud. Journ. de Physiol. et de Pathol.

16. Recklinghausen: Handbuch der Allgemeinen Pathologie.

17. Ræmer: Ueber Retinitis Hæmorrhagica In Folge von Arteriitis Proliferans. Archiv. fuer Augenheilkunde 38-iii s. 209.

Endarteriitis und Phlebitis Proliferans, etc. Bericht ueber die 27 Vers. d'Ophthalmol. Gesellshaft zu Heidelberg, s. 255.

18. Silex: in Virchow's Archiv. x s. 170.

19. Thoma: Zur Kentniss der Circulationstœrung in der Niere bei Chronischer Interstieller Nephritis. Virchow's Arch. lxxi, 1877.

20. Wagner: Virchow's Archiv. xii s. 218.

21. Weeks: Beitrag zur Pathologie der Retinitis Albumenurica.

22. Wehrli: Archiv. fuer Augenheil. xxi s. 54. Archiv. fuer Augenheilk. xxxvii s. 173.

23. Yamashita: Beitrage zur Aetiologie und Pathologischen Anatomie der Netzhautablœsung bei Retinitis Albumenurica. Inaug. Diss. Rostock, 1900.

24. Zenker und Heymann: Ueber Amaurose bei Morbus Brightii und Fettdegeneration der Retina. v. Graefe's Archiv. 2-ii s. 142.

---

## PRIMARY GLAUCOMA.

J. F. Townsend (*Jour. of South Carolina Med. Ass.*, Oct., 1907), after considering the anatomy and physiology of the eye, calls attention to the three routes by which the aqueous humor leaves the eye, viz.: 1. By way of Schlemm's canal. 2. Through the anterior surface of the iris. 3. Through the ciliary body. He believes that sclerotic changes in these filtering membranes of the eye and of the ocular blood vessels play a larger role in the production of primary glaucoma than is now generally supposed. He also thinks that not only is the lymph in the aqueous chamber at fault but also the lymph circulation in the vitreous chamber is faulty. Since glaucoma is most likely to occur during the presbyopic period he warns physicians to be on the lookout for glaucoma as a possible cause of rapidly increasing presbyopia.

# PRIMARY EPIBULBAR MELANOTIC TUMOR.*

By Julius H. Gross, M.D.,
St. Louis, Mo.

When a case of malignant epibulbar tumor presents itself, the questions we try to decide are: How deep has it extended, has it penetrated into the globe, and can it be removed without sacrificing the eye? Neither is it surprising that the thought of enucleation comes after having read, or seen, a case such as the following one reported by Dr. Otto Von Sicherer in the *Zeitschrift für Augenheilkunde,* of 1907.

I shall take the liberty of abstracting and translating this case here.

A female aged 68 came to Dr. Von Sicherer in 1900 for cataract of left eye. The right eye was blind as a result of iridocyclitis, atrophy of iris, seclusio and occlusio of the pupil. However there was no increased tension nor irritation. In both eyes surrounding the cornea there were naevi pigmentosi as large as lentils or even peas, which had been there since her earliest childhood. Without signs of inflammation and without anoyance to the patient in 1902 the naevi of the right eye began to grow noticeably. In the beginning the patient refused an operation. After about two years the tumors which were of brownish black color had grown so large that the eye could no longer be closed. The patient was unwilling to consent to a general narcosis, nor to an enucleation; even though she had been warned that the tumor was a danger to her life. Consequently only the anterior half of the globe was excised. After a few weeks the tumor had again grown to such an extent that closure of the eyelids became impossible. Soon it protruded through the palpebral opening, the surface became ulcerated, frequent and severe hæmorrhages occurred. Finally the whole orbit was filled by the tumor masses, and the pain became more and more unbearable. During the summer of 1906 the neoplasm still increased in size so that it eventually protruded from the orbit, as large as an apple, and had a moist, shining, ulcerated, crumbling, secreting surface. Her condition became constantly more tormenting. In consequence of metastases severe pain in the region of the liver developed, œdema of the legs and ascites appeared, the emaciation of the body increased, the complexion be-

*Read at the February meeting of the St. Louis Ophthalmological Society.

came still sallower, week by week the strength failed, and in August, 1906, the patient died of the general cachexia.

Fuchs in his text book (7th edition) reports a very similar case.

According to Saemisch in the latest editions of Graefe-Saemisch:

"As primary malignant growths of the conjunctiva, we have sarcoma and epithelioma. Both most frequently have their origin in the so very vascular limbus of the conjunctiva, especially on the temporal side. From this site they extend over the bulbar conjunctiva as well as over the cornea. They are on the anterior surface of the globe and in consequence are designated as epibulbar tumors. Of these tumors it is characteristic, that their growth is not accompanied by swelling of the lymphatic glands in their vicinity, that they do not disturb the general health, usually grow but slowly, above all that they seldom invade the interior of the eye; on the other hand that they have an extraordinary tendency to recur.

"Metastases seldom occur. In this the epibulbar sarcoma differs strikingly from the intraocular; which, because of its well known tendency to form metastases, is so exceedingly dangerous. Sarcoma and epithelioma may be, or may not be pigmented; however, the epithelioma is only exceptionally pigmented, whereas the sarcoma much oftener contains pigment. There is as yet no agreement as to the proper classification of the primary malignant tumors of the conjunctiva. The primary reason for this is that both forms of tumor may show an alveolar structure such as is typically found in carcinoma, and furthermore, and this is to be emphasized, that the cells which fill the alveoli may be epithelioid in character, even though they be of mesodermic origin. For instance, the sarcoma carcinomatoides of Virchow.

"The epithelial nature of these growths can be determined only when it can be shown that they have been developed from the epithelial layer. Sarcoma of the conjunctiva may be counted among the diseases of the eye which occur very seldom. It was found only eight times in a series of 45,000 cases of diseases of the eye in Norway, by Lyder Borthen. Its usual site is at the limbus of the cornea, and it generally appears as a solitary tumor. It is noticed early because of the conspicuous position of this favored site. Not so seldom there has been for some time a scarcely noticeable little dark spot, which slowly began to

grow and then in a short time increased in circumference with striking rapidity. In other cases a grayish red elevation appeared on the hitherto normal appearing corneal limbus. The surface of the gradually growing swelling is even or lobulated. Not rarely there are hæmorrhages from it. Often the sarcoma has a broad base, or at least appears to have, by which it, as a rule, rises abruptly in the corneal region, to descend gradually toward the conjunctiva. However cases have been observed in which the sarcoma had grown stalk-like from the globe. This is strange, as the benign tumors of the conjunctiva are usually polypoid in form, whereas the malignant generally have a broad base. The tumor may be pigmented or colorless. The former is usually the case, still the pigmentation may be very uneven, and may vary in the individual parts of the tumor. The intensity of the coloring of the melano-sarcoma varies between deep black and light gray.

"The dark color may also be speckled. If the tumor is very dangerous there is mixed with the grayish black color a reddish tinge. In exceptional cases only is the sarcoma without color and in contradistinction to melano-sarcoma, it is then termed leuko-sarcoma. It is remakable that the melano-sarcoma may recur as a leuko-sarcoma and vice versa. Of value in the prognosis as well as in the treatment of epibulbar sarcoma are the relations which it bears to the tissues which it covers. It usually grows from the conjunctiva at the point where this is firmly connected with the subjacent sclera and corneal limbus. It now spreads more and more on the conjunctiva without growing to the sclera; so that for some time it may be moved over the sclera. Still more important is its relation to the cornea. It seldom invades the corneal substance and when it does, only after it has existed for some time and then only via the limbus. It may cover the entire cornea beneath the epithelium without penetrating the lamina elastica anterior. It has seldom been noticed to penetrate into the globe; however, it may penetrate via the vessels. Very rarely indeed does sarcoma grow from the cornea proper. Very seldom does it penetrate the sclera. But it does spread on the surface; spreads into the eye-lids and then forms metastases. Sarcoma of the conjunctiva may arise from disease of the vessels of the conjunctiva or sclera, or from disease of the lymph vessels and lymph spaces of the episclera.

"In these cases the tumor may or may not be pigmented, and if pigmented, the pigment is derived from blood pigment. Sar-

coma of the conjunctiva may grow from a pigmented naevus. In these cases, and they are the usual ones, the sarcoma contains pigment. The naevus pigmentosus may remain stationary for a shorter or longer period and then rapidly grow into a melano-sarcoma."

Saemisch believes that whenever possible an effort should be made to preserve the eye. He cites the cases, in which there was no recurrence, reported by: Adamük, Pflüger, Hirschberg, Silex, Weinbaum, Saemisch and Noyes.

Cases in which there was no recurrence have also been reported by S. B. St. John (Trans. Am. Ophthalm. Soc., 1898).

Jackson (after case of Veasey, Trans. Am. Ophthalm. Soc. 1907).

Saemisch also mentions a case reported by Berthold in which the eye was enucleated and the subsequent examination showed that the tumor could have been removed and the globe preserved.

Similar cases have been reported by Allyn (Veasey's case, Trans. Am. Ophthalm. Soc., 1907) and Marple (*Ibid*).

Fuchs says: "The radical removal of epibulbar epitheliomata and sarcomata with preservation of the globe becomes impossible when they have spread over so much of the surface, that a large part of the conjunctiva would have to be sacrificed. There would then result such a large scar with contractions and fixation of the globe, that it would be useless; and it is better to enucleate in the beginning. The globe must also be sacrificed when the neoplasm has spread into the deeper tissues; which is most apt to take place near the anterior ciliary vessels."

Noyes in his text book says: "Sarcoma either white or pigmented (of the conjunctiva) may appear, and while removal of the disease without sacrificing the globe is to be preferred, such a course is not always possible. Complete removal is imperative and that will often compel loss of the eye."

Leber, in the Bericht über die 27te Versammlung der Ophthalmologischen Gesellschaft, Heidelberg, 1898, page 317, reports two cases of congenital melanomata which were becoming malignant in which he could clearly trace the growth of the youngest cells to the epithelium. He concluded by saying that he had come to view these tumors as descendants of the epithelium.

Axenfeld and Greef prefer to classify these tumors as sarcomata, although Greef in writing about alveolar sarcoma says: "In isolated cases the epithelial character of the enclosed cells is so plain that we may designate them as sarcoma-carcinomatoides (Virchow)."

Panas has taken the view that most of these malignant growths are epitheliomata; both in his text book, and more recently in an article in the *Archives d'Ophtalmologie* (January, 1902). In this article Panas says: "If we consider that the tumors in question arise from a dermal surface, the conjunctiva; and that the adjacent cornea and sclera beneath are not early involved, we are led to admit the epithelial, or cancroid nature of the affection; to judge of them by what takes place in the skin, in the mucous membrane of the mouth, the stomach, intestine, uterus and others. Not that sarcomata may not grow there, but they are in reality rare. Another argument which pleads in favor of this nature is that the patients have usually passed the fortieth year." And finally he cites in favor of his view the fact that naevi, polyps, and other benign tumors may become cancroid.

Ribbert, Professor of Pathology in Göttingen in his Geschwulstlehre (1904) says: All melanomata, whether of the skin or of the eye must be placed in a single group. Secondly, these tumors must, because of their characteristic behavior, necessarily be traced to certain cells in which the ability to form pigment is inherent. We must not think that a new growth of any kind may now and then form pigment. The melanoma is a typical neoplasm, just as typical as any other. As the chondroma develops from a proliferation of cartilage cells, the carcinoma from a proliferation of the epithelium, so the melanoma develops from a proliferation of the pigment cells, the chromatophores (Chromatophoren), therefore I call the growth chromatophoroma (Chromatophorom). He states that if one wishes to confirm his statements it will be necessary for him to examine fresh specimens, which have been "teased" so as to isolate the cells.

The negative results that some have obtained may be explained by the fact that they did not make use of this method. But in sections the chromatophores are not so well seen because the knife very easily cuts them, and severs the processes. As the chromatophores have many long processes we always see only a part of the cell. Wherever they form masses, they have in addition to the fully developed form a simpler form. Above all we find them in the eye in the simpler form resembling spindle cells. Therefore pathologists have been fond of speaking of pigmented spindle celled sarcomata, and thereby committed an error, which has greatly contributed to the mistake of not recognizing the chromatophoroma. These cells appear in a section as ordinary spindle cells; however, where they are isolated at

the edge of a section we can see that they have a peculiar characteristic form. This characteristic form is ribbon-like, only the middle portion containing the nucleus is swollen, spindle-like; therefore not such as have short processes which end in a sharp point. These ribbons (Die Bänder) or band-like cells are sometimes branched, and the cells thus pass through intermediate stages to those that send out processes on all sides, the chromatophores. In places where very rapid growth takes place the band-like form may be less well marked and the cells be more spindle-like. In addition to these elongated cell forms there are round, polymorphous cell elements with short plump processes. Hence a "teased" preparation will show many variations. Those showing the least variation, as a rule, are the tumors of the eye. In them we find cells with processes, band-like cells, and round cells; the latter are most deeply pigmented, the others less and not all evenly.

After very detailed descriptions of melanotic tumors and the forms which the chromatophores assume, Ribbert takes up and discusses the chief objections which have been offered to his assertions.

Wiener states that it had long since been recognized that the majority of melano-sarcomata developed from pre-existing pigment cells.

Ribbert denies this and calls attention to the fact that it has been customary to speak of pigmented sarcomata and spindle-celled sarcomata, and in so doing wished to express that the pigmentation was nothing essential, but only additional. "Certainly here and there the relationship of normal chromatophores to melanomata is mentioned, but never, before my representation, has the relationship been applied to a distinct class of tumors. One needs only to examine the literature in order to see that, excepting Payr, no one has accepted my representation. His opponents have said that the pigment cells are ordinary connective tissue cells which have become active in forming pigment."

Ribbert acknowledges that the chromatophores are of the same nature as the connective tissue cells, but says that they are peculiarly and characteristically differentiated. "The endothelial cells of the lymphatic channels are also connective tissue cells, still they represent a separate independent kind of cell. To fully appreciate this fact one need only to examine the chromatophores of the iris and the choroid. No one would take them for

ordinary connective tissue cells. Secondly, however, the chromatophores are characterized by their peculiar characteristic pigmentation. Without a doubt their pigment arises in a manner different from the ordinary blood pigment. It looks different, too; it is of a deeper brown, often dirty grayish brown. It has been thought possible to prove in a chemical way that the melanotic pigment has not the same composition as blood pigment. According to this point of view it contains no iron but sulphur which gives evidence that it is derived from albuminous substances out of which the tumor cell makes the color product."

H. G. Wells in his work on Chemical Pathology (1907) says: "Melanin occurs normally as the coloring matter of hair, of the choroid, of the skin, in the pigment matter of many lower animals, and most strikingly as a defensive substance in the 'ink' ejected by squids to render themselves invisible in the water. Pathologically melanin occurs chiefly as the result of an excessive production of this pigment by cells normally forming it, as in freckles, melanotic tumors and Addison's disease (probably). Cells that do not normally form melanin probably do not acquire this power in pathological conditions. Melanin seems always to be produced through metabolic activity of specialized cells. The idea which was formally advanced that it is derived from hæmoglobin as a product of disintegration seems to have failed entirely of substantiation."

"Tumor melanin does not differ from melanin produced by normal cells in any essential respect. Iron is frequently found microscopically in the pigment in melano-sarcoma, but is chiefly due to admixture of blood-pigment coming from extravasations of blood. The frequent occurrence of melanuria and melanæmia in patients with melano-sarcoma is not due to any peculiar property of sarcoma melanin, but to the enormous quantity of melanin that is produced by the tumor and set free in the degenerating portions. In the decomposition of hæmoglobin the first step is the splitting of the globin (which does not form pigments) from the hæmatin, from which many pigments may be derived. Hæmatin is found frequently as an amorphous, dark-brown or bluish black substance in large, old extravasations of blood, but seldom in small hæmorrhages. Wherever it is formed its duration is transient, for it gradually splits up into an iron free pigment (hæmatoidin) and an iron containing pigment (hæmosiderin). Hæmatoidin may be found in old, large extravasations, as orange colored, or red rhombic plates, first described by Vir-

chow. Sometimes, however, hæmatoidin occurs in the form of yellowish granular masses. Hæmosiderin is relatively insoluble, and therefore, is more slowly removed when formed in hæmorrhage, and more abundantly deposited in the tissues, when formed after excessive hæmolysis. According to Neumann, hæmosiderin is produced only under the influence of living cells, and in the presence of oxygen, while hæmatoidin arises independent of cellular activity. Unstained hæmosiderin generally appears in the form of brown, or yellowish brown granules, and not as crystals."

Raehlman in an article on the Pigment Epithelium of the Retina goes quite thoroughly into organic pigmentation (*Zeitschrift f. Augenheilkunde,* 1907). He says: "We must acknowledge, if we believe that it has been proved that the pigments are derived from hæmoglobin, that within the tissue a working over or change (Umsetzung) of the chromogens, brought by the blood, with the products of the cell activity, of that tissue, takes place through which the characteristic pigment of that tissue is formed. In this sense it would especially make more comprehensible the pigment formation in the epithelium, and in melanotic tumors. Looking at it in this manner the pigmentation would result in a manner analogous to the formation of the coloring of the leaves and flowers of plants. Of significance, it seems to me, in the formation of the coloring of organic tissues are the combinations which result when the coloring matter of plants or their chromogens combine with various albumins. The ultra-microscope sheds new light on the formation of such reactions. If we take solutions of coloring matter whose smallest particles are visible ultra-microscopically and bring them into the presence of albumin and then again into the presence of nuclein solution, we see how two different colors result. With the ultra-microscope the albumin and nuclein, and also the color are seen to be composed of the smallest particles. If we bring the two solutions together we see a colorless albumin particle and a color particle unite, and at the same time the color changes. In the blossoms of plants there are often two or more colors side by side, often very sharply defined (haarscharf getrennt). If we assume that there are various albumins or albuminous bodies deposited in spots in the leaves, and the chromogen is brought by the sap stream, it will combine with the albumin or starch-like bodies and form various colors.

In the feathers of birds we find something very similar taking place.

Now to our case:

M. F., female, age 21 years, of medium stature, dark brown hair, dark brown eyes, presented herself May 27th, 1906, because of a growth at the nasal limbus of right cornea. Family history good. No history of neoplasm or any other hereditary predisposition. Patient has never had any trouble with her eyes. No history of any injury. Previous general health good. About 6 months ago members of her family noticed something like a scratch at the nasal limbus in the horizontal meridian of the right cornea; soon after this the small black mass of the tumor was noticed. Since it was first noticed it had grown slowly but steadily. For the last 6 months or so she has not been feeling well, no particular complaint, just a general indisposition. One year ago she weighed 148 pounds, but now weighs only 122. In the horizontal meridian of the right eye at the nasal limbus of the cornea there is a black growth, measuring 2 mm. in the vertical 1.5 mm., in the horizontal meridian and rising above the level of the globe about 1.5 mm. The growth rises abruptly at the corneal side to descend gradually to the conjunctival end. The base is somewhat constricted so that the edges protrude flap-like over the base. It is firmly and immovably attached to the corneal limbus. Its color is a shining black. There is no increased vascularization near the tumor or elsewhere on the globe. The color of the iris is a dark brown. There are no naevi pigmentosi, or pigment spots noticeable in the circumcorneal zone. The fundus is normal and there is no sign of any growth in the eyes or elsewhere so far as I was able to ascertain. With the kind advice and under the direction of Dr. A. E. Ewing the tumor was removed in the following manner: the tumor was firmly grasped with forceps and trimmed off of the cornea with a double edged round pointed knife having its cutting edge at the end. In like manner it was cut off the sclera, the site of the wound was then carefully curetted with the knife, and a small suture placed in the conjunctiva. The wound healed nicely with scarcely a scar. There has been no recurrence at this date (after 20 months). The vision is as good now as before the operation.

In 1880 Noyes published a list of 127 cases of epibulbar tumors which had been reported (*Archiv. f. Augenheilk.* IX., p. 127).

In 1886 Remak collected and published a list of 39 epibulbar tumors which had been reported since Noyes' publication (*Archiv. f. Augenheilk.* XVI. p. 276).

In 1902 Panas published a list of selected cases (*Archives d'Ophtalmologie,* Jan., 1902, Vol. XXII).

In 1903 Verhoeff and Loring discussed and analyzed the previously published cases (*Archives of Ophthalmology* XXXII., 1903).

Microscopic examination shows that the tumor is covered by the epithelium, which does not dip into the growth. There are three well defined pigmented areas of dark brown color in which there are many cells, of medium size, containing pigment; there is also pigment in the inter cellular substance. Surrounding these areas there are many smaller roundish cells which make up the greater part of the tumor. The tumor cells are invading the conjunctival tissue. The blood vessels are not very numerous. The pigmented cells are chromatophores, and the smaller round cells are also chromatophores which have not developed pigment.

In concluding I wish to express my thanks to Drs. Green, Ewing, and Tiedeman for valuable suggestions, and for the use of their literature; and Dr. Luedde for the preparation of the microscopic specimens.

BIBLIOGRAPHY.

**Zeitschrift fuer Augenheilkunde, 1907.**

**Fuchs, Lehrbuch der Augenheilkunde.**

**Graefe-Saemisch, Handbuch der Gesammten Augenheilkunde. (2nd Edition).**

**Transactions of the American Ophthalmological Society, 1898 and 1907.**

**Noyes, a Text book on Diseases of the Eye. (2nd Edition).**

**Leber, in Bericht ueber die 27te Versammlung der Ophthalmologischen Gesellschaft, Heidelberg, 1898.**

**Lehrbuch der Speciellen Pathologischen Anatomie von Johannes Orth.**

**The Pathology of the Eye, written by Greeff.**

**Panas, Archives d'Ophtalmologie, Jan., 1902.**

**Ribbert, Geschwulstlehre, 1904.**

**H. G. Wells, Chemical Pathology, 1907.**

# OBITUARY.

## HERMAN SNELLEN.*

February 19th, 1834—January 18th, 1908.

By D. M. Straub.

Translated by Adolf Alt, M.D.

On January 18th, 1908, died at Utrecht, at the age of 73 years, Herman Snellen, honorary professor of ophthalmology in the University of that city.

A pupil of Donders, Snellen in turn became the chief of the Netherlandic school. He took a great part in the development of ophthalmology in the second half of the 19th century and his works occupy an important part.

In his position as professor and chief of a large clinic, during his long life so full of earnest work, he promulgated the new doctrines and applied their practical results for the benefit of the patients.

Snellen was graduated as Doctor of Medicine at the University of Utrecht on July 4th, 1857. His thesis was remarkable. Donders had indicated to him as a subject the experimental neuroparalytic keratitis. By means of happy and useful modifications of the fundamental experiments of Magendie, Snellen arrived at new and unexpected results which reopened the question of the doctrine of trophic inflammations.

Before finishing his medical studies, Snellen had associated himself with Donders in his ophthalmological researches. In 1858 the celebrated Netherlandic Eye Hospital was inaugurated at Utrecht, of which Donders was the founder and first director, Snellen the first interne. Thus a large field was opened to him for applying in his daily practice of ophthalmology the discoveries made, thanks to the invention of the ophthalmoscope. He was inspired in the execution of his art by the physiologic works of Helmholtz and Donders, the large clinical views of Albrecht von Graefe, Bowman and Arlt. In 1862, till then extraordinary professor, he was called to fill the chair of physiology at the University of Utrecht. From this time he relinquished to

*Annales d'Oculistique, Feb., 1908.

Snellen the greatest part of his practical ophthalmic work. True, Donders remained in title the Director of the Netherlandic Eye Hospital till 1884, but Snellen had in fact been director of the clinic for a number of years before Donders resigned these functions. From 1877 to 1899 Snellen occupied the chair of ophthalmology in the University of Utrecht, which had been created for him. After retiring from the professorship he remained for another four years the director of the new clinic of Utrecht. His oldest son is his successor in both positions.

As long as Snellen's activity lasted, the Utrecht clinic was a point of attraction for a multitude of young oculists from all parts of the world, who came to do physiological work in Donders' laboratory and to follow the lectures and consultations of Snellen at the Netherlandic Hospital. Pupils of Snellen and oculists, they carried his great reputation of clinician and practitioner all over the world.

The culminating point of Snellen's scientific work was the study of the visual acuity which led to the well-known famous formula and the edition of the optotypes which have found a place in every clinic of the world and have remained models. The development of the methods of examining the eye was Snellen's favorite scientific field.

From the last epoch of his life date his Bowman lecture on vision and retinal perception (1896) and the paper read at the Congress at Brussels (1897) on the quantitative determination of the color sense. In his youth he had created instruments in order to measure the introcular tension and apparatus to detect simulation and unilateral amblyopia. From this period date his focometer and his instruments to determine astigmatism and to measure strabismus. Thus he was the man designed to edit, in collaboration with his friend Landolt, the volume of the first edition of the Graefe-Saemisch Cyclopedia, which treats of the methods of eye examination. A second edition of this work appeared somewhat later in the complete Treatise of Ophthalmology of De Wecker and Landolt.

In practical ophthalmology Snellen concentrated his attention on the development of methods of operation. His operative measures for remedying the malposition of the eyelids had the rare success of being accepted in all clinics. For the second edition of the Graefe-Saemisch Cyclopedia he undertook to write a volume on eye operations. This task remains unaccomplished.

Snellen did not only execute his operations with an elegant and sure hand, but, what is perhaps even more important, in the case of misfortune and accident he did everything to remedy the conditions with a patience and devotedness above praise.

I must add two traits to this rapid sketch of the personality of the great master: his amiability in personal contact and his talent of organization. These two qualities have largely contributed to the remarkable success of the international congress of Ophthalmology held at Utrecht in 1899, organized and presided over by Snellen. His amiability has been highly appreciated by the numerous colleagues who came to visit the classic field of ophthalmology where Snellen worked.

The Hollandish people owe to his talent of organization the founding of the new Netherlandic Hospital, called after Donders. Thanks to Snellen, there stands at Utrecht, since 1894 a building which is truly worthy of the great founder of the Netherlandic School of Ophthalmology. Its exterior appearance gives more the idea of a palace than of an ophthalmic clinic.

---

# ABSTRACTS FROM MEDICAL LITERATURE.

By W. A. Shoemaker, M.D.,

St. Louis, Mo.

## NEGATIVE INFLUENCE OF MERCURIAL TREATMENT OF SYPHILIS ON DEVELOPMENT OF PARASYPHILITIC NERVOUS AFFECTIONS.

P. Schuster (*Deutsche Medizinische Wochenschrift,* Dec. 12) for years has been collecting data in regard to the preceding mercurial treatment in all his cases of parasyphilitic nervous affections. In 75 cases of tabes with a verified history of syphilis, only 17 (22.7 per cent.) of the patients had never had mercurial treatment; 31 (41.3 per cent.) had taken a single course; 13 (17.3 per cent.) two courses, and 14 (18.7 per cent.) had had from three to eight courses. In 35 cases of paralysis after verified syphilis, only 3 (8.6 per cent.) of the patients had never had specific treatment; 21 (60 per cent.) had taken a single course; 5 (14.3 per cent.) had taken two courses, and 6 (17.1 per cent.) had records of from three to nine courses.

In 76 cases of cerebro-spinal syphilis, 10 (13.2 per cent.) of the patients had never had mercurial treatment; 36 (47.4 per cent.) had had one course; 15 (19.7 per cent.) two courses, and 15 from three to six courses. No cases are included in these statistics except those in which the records of the syphilis and of the treatment were verified as authentic. A surprising fact brought out by this study is that the interval between the primary lesion and the development of the nervous trouble was not lengthened by the mercurial treatment. On the contrary, the interval was longest in the untreated cases and briefer in proportion to the number of courses that had been taken. In Eulenberg's 27 tabetics the nervous trouble first manifested itself after an average interval of 12.4 years among the 13 untreated patients; after 9.3 years in the 11 patients who had taken a single course, and after 5 years in the 3 who had had from two to four courses. In Dinkler's 49 cases the intervals were respectively 11.7 years, 10.6 years and 6.5 years. The range in Schuster's 75 tabetics was from 13.4 years in the untreated to 7.9 years in the cases in which the largest number of courses had been taken. In paralysis also there was nothing to indicate that the interval had been prolonged by the mercurial treatment. From all this material Schuster draws the conclusion that the evidence is against the assumption that mercurial treatment wards off or retards the "metasyphilitic" nervous affections. The evidence seems, rather, to favor the view that these nervous affections are the work of the anti-bodies of syphilis, and that the syphilitic virus itself is not responsible for them. Biologic tests have shown that mercurial treatment does not expel the antibodies from the blood. The clinical picture of tabes and paralysis is the same whether the formerly syphilitic patient received mercurial treatment or not, while clinical and biologic evidence is accumulating to sustain the theory that the nervous after-affections of syphilis are caused by the anti-bodies generated in the course of the disease, and on which mercury seems to have little influence.—*Jour. A. M. A.*

## THE PATHOGENESIS OF IRIDO-CYCLITIS.

Sidney Stephenson (*The Ophthalmoscope,* Oct., 1907) believes that it is justifiable to claim that every case of irido-cyclitis is of septic or toxic origin. The septic infection may be either exogenous or endogenous. Infection accompanying ulcer of the cornea or injuries are examples of the exogenous form, while

syphilis, gonorrhœa, rheumatism, tubercle, leprosy, pneumonia and pyorrhœa alveolaris are all instances of the endogenous type. The poison, whether it be micro-organism, or toxin, circulating through the blood, an attempt is made by the ciliary processes to excrete it, the aqueous thus being contaminated, by which an inflammation of the tissues—ciliary body and iris—is excited. Bearing out this view is the fact that treponema pallidum, tubercle bacillus, Poynton's micrococcus rheumaticus, typhoid bacillus, and streptococcus have all been found in the aqueous cases of irido-cyclitis caused by these different infections. The relapsing forms of irido-cyclitis associated with rheumatoid arthritis and antecedent gonorrhœa and influenza may be caused by the germs of these diseases lying latent until altered conditions favored their renewed activity. If the germs are thus excreted by the ciliary processes it is reasonable to suppose that toxins are likewise removed from the blood current into the aqueous, although it is much more difficult to demonstrate their presence in this fluid. Stephenson thinks this theory a good working hypothesis, at least, in the management of inflammations of the iris and ciliary body.

## BACTERIOLOGIC ASPECTS OF NEUROPATHIC KERATITIS.

Davis and Hall (*British Med. Jour.,* Jan. 11), after investigating this subject, concludes that three factors are present in the production of neuropathic keratitis: 1. Removal of the Gasserian ganglion. 2. The presence of the bacillus. 3. A factor of undefined nature dependent on the eyelids and removed by closing them. The first two factors are not sufficient in themselves, as suturing the lids together prevents or cures the keratitis. The first and third are not adequate without the second as, with these two conditions present, keratitis does not follow unless the organism be present, and occurs in the same proportion of patients as that in which the organism occurs in normal persons.

## GLAUCOMA IRIDECTOMIES.

G. A. Berry (*Edinburgh Med. Jour.,* Nov., 1907) believes that iridectomy is capable of permanently arresting glaucoma at all its stages and in whatever form it makes its appearance. It is less likely to be successful, the longer the disease has existed, regardless of the damage that has been done. Hence the opera-

tion should be done as soon as possible after the certain diagnosis of the disease, and should be tried as a first measure in all stages of the disease. Miotics should be used after operating and should be continued indefinitely. The incision should be made with a keratome and placed as peripherally as possible with safety. It is not necessary to remove as much iris as von Graefe originally advised. A cystoid cicatrix should be formed in cases that do not respond to iridectomy followed by miotics. In doing this the section into the eye should be made so as to include the tissues behind the root of the iris.

## SURGICAL TREATMENT OF DETACHED RETINA.

G. W. Maser (*The Medical Fortnightly,* Oct. 25), following Lang's method, has operated on four patients with detached retinæ, in three of whom he has succeeded in restoring sight. The operation is successful only when the detachment is caused by the accumulation of serum between the retina and choroid, so that the cases must be selected. The objects of the operation are to allow the escape of the serum and to produce a ragged wound in the retina which is followed by sufficient inflammation and exudation to unite the retina to the choroid. The method of operating follows: A triangular flap is made in the conjunctiva between the recti muscles. After the hæmorrhage ceases a von Graefe cataract knife is passed through the sclera, choroid and retina and into the vitreous. Then by slightly turning the knife the serum drains off after which the retina is further incised. By turning the knife as nearly at a right angle as possible the retina is again cut, thus producing a wound which is followed by considerable inflammation and usually by reattachment of the retina at this point but not of the entire retina if more than half had been detached. A second and even a third operation may be done at different points after the inflammation following the preceding one has subsided. No dangerous reaction has occurred in any of his cases and his experience has been most encouraging.